

⑤

Int. Cl. 2

A 61 K 7/00

A 61 K 7/16

A 61 K 7/48

A 61 K 9/68

⑤ BUNDESREPUBLIK DEUTSCHLAND

DEUTSCHES



PATENTAMT

DT 26 08 226 A 1

⑪

Offenlegungsschrift 26 08 226

⑫

Aktenzeichen.

P 26 08 226 8

⑬

Anmeldetag.

28. 2. 76

⑭

Offenlegungstag

8. 9. 77

⑮

Unionspriorität:

⑮ ⑬ ⑪

⑯

Bezeichnung: Mittel mit physiologischer Kühlwirkung

⑰

Anmelder: Haarmann & Reimer GmbH, 3450 Holzminden

⑱

Erfinder: Bauer, Kurt, Dr.; Bröning, Jürgen, Dr.; Grüb, Helmut, Dr.;
3450 Holzminden

DT 26 08 226 A 1

- [51] Int. Cl.²: A 61 K 7/00
A 61 K 7/16
A 61 K 7/48
A 61 K 9/68
- [19] Federal Republic of Germany
- [11] Patent (Offenlegungsschrift) 26 08 226
- [21] File Number: P 26 08 226.8
- [22] Application Date: February 28, 1976
- [43] Disclosure Date: September 8, 1977
- [30] Union Priority:
- [71] Applicant: Haarmann & Reimer GmbH, 3450 Holzminden
- [72] Inventor: Bauer, Kurt, Dr.; Brüning, Jürgen, Dr.; Grüb, Helmut, Dr.; 3450 Holzminden
- [54] Title: AGENT WITH PHYSIOLOGICAL COOLING ACTION

AGENT WITH PHYSIOLOGICAL COOLING ACTION

The invention relates to agents with physiological cooling action on the skin and mucosae of the body.

Menthol, the chief constituent of peppermint oils, features an excellent cooling action on skin and mucosae. Its cooling action is not based on latent heat of evaporation but rather arises through direct action of the compound on the nerve ends of the cold receptors. The odor and taste properties of menthol, however, limit, and in some cases preclude, its use. The peppermint odor is too specific and too sharp and irritating to the mucosae and conjunctivae for various applications. For other applications, the flavor is too sharp and bitter. The high volatility of menthol also frequently has adverse effects.

Therefore, there have been numerous attempts to find substances that possess the positive effect of the cooling action without the above-described disadvantages of menthol. For example, *p*-menthane-3-carboxamide and esters of *p*-menthane-3-carboxylic acid are proposed in DT-OS 2 202 535, *N*-substituted *p*-menthane-3-carboxamide in DT-OS 2 205 255, substituted amides in DT-OS 2 317 538, cyclic and acyclic sulfoxides in DT-OS 2 334 985, and substituted phosphine oxides in DT-OS 2 345 156.

These compounds, which in some cases come very close to the goal of having a cooling action while being odorless and tasteless, have, however, the disadvantage that they are neither natural substances nor can they be degraded by the human organism to natural substances. Therefore, they are unsafe physiologically and in terms of food law. Furthermore, some are very expensive, since they can be produced only in multi-stage processes.

The menthol derivatives proposed heretofore, which either occur naturally or are degraded into natural substances by the organism, do not completely satisfy the imposed requirements. For example, the 1-menthyl ethyl carbonate proposed in DT-OS 2 022 364 has an orangelike odor; the *N*-

acetyl glycine menthyl ester proposed in DT-OS 2 433 165 and the menthol esters of heterocyclic carboxylic acids proposed in DT-OS 2 339 661 are bitter, and the menthyl keto esters proposed in US-PS 3 830 930 are in some cases lingeringly bitter and do not have the desired cooling action.

It has now been found, surprisingly, that esters of menthol and naturally occurring hydroxycarboxylic acids with 2-6 carbon atoms, which are optionally esterified at the hydroxy group of the carboxylic acid, are odorless and tasteless and have excellent, particularly long-lasting cooling action.

The invention therefore relates to agents with a physiological cooling action on the skin and mucosae of the body, which are characterized by the fact that they contain esters of menthol and naturally occurring hydroxycarboxylic acids with 2-6 carbon atoms, which are in turn optionally esterified at the hydroxy group with carboxylic acids having 1-4 carbon atoms.

Examples of naturally occurring hydroxy carboxylic acids with 2-6 carbon atoms are glycolic acid, β -hydroxybutyric acid, α -hydroxyisovaleric acid, α -hydroxy- α -methylvaleric acid, α -hydroxy- γ -methylvaleric acid, α -hydroxycaproic acid and β -hydroxycaproic acid, but particularly lactic acid.

Carboxylic acids with 1-4 carbon atoms with which the hydroxy groups of the hydroxycarboxylic acids can be esterified include particularly formic acid, acetic acid and propionic acid.

Only some of the esters to be used in accordance with the invention are new. However, the esters described were not known to have a physiological cooling action on the skin and mucosae of the body. Esters can be produced by conventional methods, for example, by acid-catalyzed esterification of menthol with hydroxycarboxylic acids or by reduction of ketocarboxylic acid menthyl esters. Ketocarboxylic acid menthyl esters can be obtained, for example, by interesterification of ketocarboxylic acid alkyl esters with menthol. The interesterification of the hydroxy group of the hydroxycarboxylic acid with the carboxylic acids having 1-4 carbon atoms is preferably conducted as the last stage.

The esters to be used in accordance with the invention have asymmetric carbon atoms; therefore, optical isomerism can occur in them. Depending on the starting material and the production methods used, they can also be present as mixtures of the optical isomers or as pure isomers. The cooling action of the isomers may vary, so one or the other isomer can be preferred.

The inventive cooling agents can be used wherever a physiological cooling action is desired. Compositions in which such cooling agents are used include foods and tobacco products such as chewing gum, chewing tobacco, cigarettes, beverages, ice cream, confections, etc; pharmaceutical preparations, personal hygiene agents or cosmetic preparations, such as toothpastes and powders, mouthwashes, gargles, perfumes, powders, lotions, ointments, oils, creams, aftershave lotions, shampoos, etc.

The final products contain the esters to be used in accordance with the invention in a quantity sufficient to stimulate the cold receptors and produce the desired sensation of coldness. As a rule, 0.1-5 wt% as against the weight of the total composition is used. Besides the cooling action, the inventive esters, particularly menthyl lactate, have an enhancing action, i.e., a taste-enhancing action for other flavors. For example, the addition of an amount of the esters used in accordance with the invention below the threshold for a physiological cooling action permits a reduction in the amount of peppermint oil, spearmint oil or other flavors added, for example, to chewing gums or mint drops without any change in taste.

The following examples illustrate the use of the inventive cooling agents in various compositions. The percentages here are percentages by weight.

Example 1. Toothpaste

The following components were mixed in the usual way:

Glycerin DAB 6	20 %
<i>p</i> -hydroxybenzoic acid methyl ester	0.15 %
Carboxymethyl cellulose	1.2 %
Saccharin	0.2 %
Dicalcium phosphate (aqueous)	48 %
Sodium lauryl sulfate	2.2 %
Flavors	1.0 %
Water	100 %

Before the mixing process was completed, 1% *l*-menthyl lactate was added. The toothpaste featured a cooling effect.

Example 2. Chewing Gum

0.3% *O*-acetyl lactic acid-*l*-menthyl ester was incorporated into a commercial chewing gum base. The chewing gum mass produces a cooling effect in the mouth.

Example 3. Fondant

1% *l*-menthyl lactate was incorporated into a commercial fondant base. The fondant has a pleasantly refreshing taste.

Example 4. Mouthwash

A mouthwash concentrate was prepared from the following components:

Ethanol	60 %
Bromochlorophen	0.05 %
Polyoxyethylene sorbitan monolaurate	1 %
Allantoin	0.2 %
Saccharin	0.2 %
Flavors	to 100 %

5% *l*-menthyl lactate was added to the mixture. The concentrate was diluted with a 10-fold volume of water to manufacture mouthwash. The mouthwash showed a cooling action.

A mouthwash with the same action was obtained using the same amount of glycol acid, β -hydroxybutyric acid, α -hydroxyisovaleric acid, α -hydroxy- α -methylvaleric acid, α -hydroxy- γ -methylvaleric acid, α -hydroxycaproic acid or β -hydroxycaproic acid-*l*-menthyl ester instead of the 5% *l*-menthyl lactate.

Example 5. Facial Cleansing Lotion

Facial cleansing lotion was manufactured from the following components:

Ethanol	26.3 %
<i>l</i> -menthyl lactate	1. %
Perfume oil	0.1 %
Emulsifier	4 %
1,2-propylene glycol	1 %
Allantoin	0.05 %
Lactic acid	0.05 %
Water	67.5 %

The lotion has a cooling action on the facial skin.

Example 6. Aftershave Lotion

An aftershave lotion was prepared from the following components:

Ethanol	55.5 %
<i>l</i> -menthyl lactate	1.5 %
Perfume oil	0.5 %
Emulsifier	0.3 %
Water	39.8 %
Allantoin	0.2 %
1,2-propylene glycol	2 %
Lactic acid	0.2 %

The lotion produces a cooling action when applied to the face.

A preparation with the same action is obtained using the same amount of *O*-formyl lactic acid-*l*-menthyl ester instead of *l*-menthyl lactate.

Example 7. Clear Shampoo

Clear shampoo was produced from the following components:

Fatty acid amidoalkylbetaine	60 %
Water	35.2 %
Preservative	0.2 %
<i>d,l</i> -menthyl lactate	2 %
Perfume oil	0.5 %
Coconut fatty acid diethanolamide	2 %

The shampoo has a strong cooling action on the scalp.

Example 8. Afterbath Freshener

An afterbath freshener was prepared from the following components:

Ethanol	50 %
<i>l</i> -menthyl lactate	1.5 %
Perfume oil	2 %
Lanolin-based oil restorer	2 %
Emulsifier	1.5 %
Water	43 %

The afterbath freshener features a pleasantly refreshing action.

Claims

1. Agents with physiological cooling action on the skin and mucosae of the body, characterized by the fact that they contain esters of menthyl and naturally occurring hydroxycarboxylic acids with 2-6 carbon atoms which are optionally esterified at the hydroxy group with carboxylic acids having 1-4 carbon atoms.

2. Agent according to Claim 1, containing menthyl lactate as a cooling-reagent.

3. Use of esters of menthol and naturally occurring hydroxycarboxylic acids with 2-6 carbon atoms, which are themselves optionally esterified at the hydroxy group with carboxylic acids having 1-4 carbon atoms, as agents with a physiological cooling action on the skin and mucosae of the body.

4. Use of menthyl lactate in accordance with Claim 3.

5. Cooling agent-containing compositions characterized by a content of cooling agents according to Claims 1 and 2.

6. Cooling agent-containing compositions according to Claim 5, characterized by the fact that they contain the cooling agents according to Claims 1 and 2 in a quantity of 0.1-5 wt% as against the weight of the preparation.